WEST Search History

DATE: Thursday, September 11, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L14	(l7 or l8) near10 (depressi$4 or antidepress$6)	123	L14
L13	l8 same l10	23	L13
L12	l6 same l8	2	L12
L11	l3 same l5	0	L11
L10	dissoc$ or refract$4 near3 depressi$4	73732	L10
L9	l1 same l3	0	L9
L8	nalmefene or naloxone or naltrexone or nalbuphine or thebaine or kappa agonist	3191	L8
L7	(opiate$1 or opioid$1) near3 antagonis$4	1756	L7
L6	(depressi$4 or antidepress$4)near5 dissocia$6	27	L6
L5	(depressi$4 or antidepress$4)near5 dissocia$6	0	L5
L4	(depressi$4 or antidepress$4)near dissocia$6	6	L4
DB=USPT,PGPB; PLUR=YES; OP=ADJ			
L3	(depressi$4 or antidepress$4)near dissocia$6	5	L3
L2	6080736.pn.	1	L2
L1	6132724.pn.	1	L1

END OF SEARCH HISTORY

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=> file medicine
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                                                           ENTRY    SESSION
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FILE 'USPAT2' ENTERED AT 12:55:46 ON 11 SEP 2003
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=> s depressi? or antideress? (s) dissociation
  30 FILES SEARCHED...
L1   1204255 DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION

=> s depressi? or antidepress?
L2   1388563 DEPRESSI? OR ANTIDEPRESS?

=> s dissocia?
L3   670508 DISSOCIA?

=> s l2 (s) l3
L4   3968 L2 (S) L3

```
=> s opiate? or opioid?
  30 FILES SEARCHED...
L5       411408 OPIATE? OR OPIOID?

=> s antagonis?

  27 FILES SEARCHED...
L6      2578933 ANTAGONIS?

=> s l5 (s) l6

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=> s opiate? or opioid? (s) antagonis?
L7       233041 OPIATE? OR OPIOID? (S) ANTAGONIS?

=> d his

     (FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
     EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
     MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP
     2003
L1      1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
L2      1388563 S DEPRESSI? OR ANTIDEPRESS?
L3       670508 S DISSOCIA?
L4         3968 S L2 (S) L3
L5       411408 S OPIATE? OR OPIOID?
L6      2578933 S ANTAGONIS?
L7       233041 S OPIATE? OR OPIOID? (S) ANTAGONIS?

=> s nalmefene or naloxone or naltrexone or nalbuphine or thebaine
L8       186472 NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAINE

=> s l4 and l7
L9           114 L4 AND L7

=> s amitriptyline or lofepramine or bupropion or citalopram or fluoxetine or fluvoxamine or
imipramine or paroxetine or sertraline or venlafaxine or nefazodone or nortriptyline or
mirtazapine or reboxetine or SAM-e
  12 FILES SEARCHED...
  28 FILES SEARCHED...
L10      253977 AMITRIPTYLINE OR LOFEPRAMINE OR BUPROPION OR CITALOPRAM OR FLUOX
                ETINE OR FLUVOXAMINE OR IMIPRAMINE OR PAROXETINE OR SERTRALINE
                OR VENLAFAXINE OR NEFAZODONE OR NORTRIPTYLINE OR MIRTAZAPINE OR
                REBOXETINE OR SAM-E

=> s l9 and l10
L11            8 L9 AND L10

=> s l10 and l8
L12         4049 L10 AND L8

=> s l4 and l12
L13           13 L4 AND L12

=> dup rem
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L14 ANSWER 1 OF 12 IFIPAT COPYRIGHT 2003 IFI on STN DUPLICATE 1
AN 10343482 IFIPAT;IFIUDB;IFICDB
TITLE: TREATMENT OF REFRACTORY DEPRESSION WITH AN OPIATE ANTAGONIST AND AN ANTIDEPRESSANT
INVENTOR(S): Glover; Hillel, New York, NY, US
PATENT ASSIGNEE(S): Unassigned
AGENT: DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP, 2101 L STREET NW, WASHINGTON, DC, 20037-1526, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003087896	A1	20030508
APPLICATION INFORMATION:	US 2001-925190		20010809
FAMILY INFORMATION:	US 2003087896		20030508

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
NUMBER OF CLAIMS: 22

AB An **antidepressant** or a pharmaceutically acceptable salt thereof, and an opiate antagonist or a pharmaceutically acceptable salt thereof, are used to treat refractory **depression** characterized by **dissociation**.

ECLM 1. A method for treating refractory **depression** characterized by **dissociation**, comprising administering to a patient in need thereof an effective **dissociation** reversing amount of an opiate antagonist or a pharmaceutically acceptable salt thereof; and an effective **depression** reversing amount of an **antidepressant** or a pharmaceutically acceptable salt thereof.

ACLM 3. The method of claim 2, wherein the opiate antagonist is selected from the group consisting of **nalmefene**, **naloxone**, **naltrexone**, **nalbuphine**, **thebaine**, and combinations thereof.

6. The method of claim 1, wherein the effective dissociation reversing amount comprises an initial dosage of **Nalmefene** in the amount of about 50 mgs. b.i.d. for about three days, followed by a dosage of about 100 mgs.. . .

11. The method of claim 1, wherein the antidepressant is selected form the group consisting essentially of **amitriptyline**, **lofepramine**, **bupropion**, **citalopram**, **fluoxetine**, **fluvoxamine**, **imipramine**, **paroxetine**, **sertraline**, **venlafaxine**, **nefazodone**, **nortriptyline**, **mirtazapine**, **reboxetine**, **SAM-E** and combinations thereof.

12. The method of claim 1, wherein the effective depression reversing amount comprises an initial dosage of **Bupropion** SR in the amount of about 100 mgs. to about 300 mgs. one time daily.

13. The method of claim 1, wherein the effective depression reversing amount comprises a dosage of **Venlafaxine** in the amount of about 75 mgs. per day to about 375 mgs. one time daily.

14. A method for treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need thereof an effective amount of (a) an **antidepressant**; and (b) an opiate antagonist.

16. The method of claim 14, wherein the opiate antagonist is selected from the group consisting of **nalmefene**, **naloxone**, **naltrexone**, **nalbuphine**, **thebaine**, and combinations thereof.

18. The method of claim 14, wherein the antidepressant is selected form the group consisting essentially of **amitriptyline**, **lofepramine**, **bupropion**, **citalopram**,

fluoxetine, **fluvoxamine**, **imipramine**, **paroxetine**, **sertraline**, **venlafaxine**, **nefazodone**, **nortriptyline**, **mirtazapine**, **reboxetine**, **SAM-E** and combinations thereof.

19. A method of treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need thereof at least one opiate antagonist; evaluating said patient for a response to said opiate antagonist; reassessing said patient for **depression**; and administering at least one **antidepressant** to said patient.

L14 ANSWER 2 OF 12 USPATFULL on STN

ACCESSION NUMBER: 2003:195316 USPATFULL

TITLE: Electroencephalography based systems and methods for selecting therapies and predicting outcomes

INVENTOR(S): Suffin, Stephen C., Sherman Oaks, CA, UNITED STATES
Emory, W. Hamlin, Malibu, CA, UNITED STATES
Brandt, Leonard J., San Juan Capistrano, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003135128	A1	20030717
APPLICATION INFO.:	US 2002-193735	A1	20020711 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-501149, filed on 9 Feb 2000, PENDING Continuation-in-part of Ser. No. US 2001-930632, filed on 15 Aug 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-304627P	20010711 (60)
	US 2001-304628P	20010711 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711

NUMBER OF CLAIMS: 62

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 15 Drawing Page(s)

LINE COUNT: 4945

DETD . . . the familiar therapeutic entities PROZAC 435 and EFFEXOR 440. Similarly, Class 2 410 include MAOI 445 and Class 3 includes **Bupropion** 450.

DETD . . . (with as many as 7% of users being even slower metabolizers, i.e., having even longer half-lives for the active ingredient **fluoxetine** hydrochloride), and (2) it is contraindicated with administration of MAOI 445 requiring an intervening period of at least 14 days. . . experimentation while the invention provides a predictive strategy for choosing an effective agent. Similarly, WELLBUTRIN, an agent in the sub-class **bupropion** 450 is also contraindicated with MAOI 445 agents. Thus, the ability to prospectively distinguish between such agents enables effective care. . .

DETD . . . atypical cardiac arrthymias including variants of sinus tachycardia, intermittent sinus tachycardia, sinus bradycardia and sinus arrthymia, cognitive problems, atypical dermatitis, **depression** , **dissociative** disorders, eating disorders such as bulimia, anorexia and atypical eating disorders, appetite disturbances and weight problems, edema, fatigue, atypical headache. . .

DETD . . . information for a number of therapeutic entities known by their generic names. Examples of such therapeutic entities include: alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion** regular and sustained release tablets, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, , deprenyl, desipramine, dextroamphetamine regular tablets and spansules, diazepam, disulfiram, d/l amphetamine, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium

carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, methylphenidate regular and sustained release tablets, midazolam, meprobamate, metoprolol regular and sustained release form, mirtazepine, molindone, moclobemide, **naltrexone**, **nefazodone**, nicotine, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol regular and sustained release tablets, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranylcypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid or **venlafaxine**.

DETD . . . the study. TABLE 8 summarizes the composition of the patient population.

TABLE 8

DSM DIRECTED	Number of Patients	Mean/24 h in mg
Fluoxetine	2	40
Nefazodone	1	300
Sertraline	2	175
Clonezapam	1	2
Lithium	2	1050
Valproate	2	1125
Average Number of Medications/Patient	1.8	

DETD [0226]

TABLE 9

DSM + EEG DIRECTED	Number of Patients	Mean/24 h in mg
Valproate	2	1000
Lithium	2	750
Paroxetine	1	30
Fluoxetine	2	35
Methylphenidate	2	27.5
Carbamazepine	2	850
Sertraline	1	100
Average Number of Medications/Patient	1.7	

DETD . . . factors affecting medical condition, atypical asthma and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, **bupropion**, pamate, moclobemide, phenalzine, seligeline, **venlafaxine**, carbamazapine, gabapentin, lamotrigine, ginko biloba, dexedrine, methapmphetamine, methylphenidate, and pemoline.

DETD . . . one of anxiety disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, buproprion, **citalopram**, **fluvoxamine**, citalopramine, clomipramine, moclobemide, pamate, phenalzine, seligeline, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, lithium, ginko biloba, kava. . .

DETD . . . childhood, or adolescence and the second treatment is selected from the group consisting of gaba glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, clomiprimine, doxepin, **fluoxetine**, **fluvoxamine**, moclobemide, pamate, phenalzine, seligeline, trazodone, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clorazepate, diazapam, oxazepam, quazepam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st.. . .

DETD . . . the second treatment is selected from the group consisting of

gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, moclobemide, pamate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, lorazepam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy. . .

DETD . . . amnestic and other cognitive disorders and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, **amitriptyline**, buproprion, fluxotine, moclobemide, parnate, phenalzine, seligeline, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, atenolol, metopolol, propranolol, lithium, ginko biloba, silbtrimin, amantadine, phototherapy at 10000 lux, zolipidem, adderall, dexedrine, methapmphetamine,. . .

DETD . . . disorders not elsewhere classified and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, clomiprimine, desipramine, moclobemide, **nefazodone**, parnate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, ginko biloba, kava kava, silbtrimin, amantadine, phototherapy at 10000. . .

DETD . . . codes and conditions and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, clomiprimine, **fluvoxamine**, moclobemide, notriptyline, parnate, phenalzine, seligeline, trazodone, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy at. . .

DETD . . . the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, moclobemide, parnate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, phototherapy at 10000. . .

DETD . . . sleep disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, buspirone, **citalopram**, clomiprimine, desipramine, **fluoxetine**, **fluvoxamine**, moclobemide, pamate, phenalzine, seligeline, **sertraline**, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine,,atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy. .

DETD . . . of somatoform disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine,. . .

DETD . . . one of substance-related disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, , **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy at. . .

DETD . . . Optionally, the treatment modality is drug therapy, and wherein the drug is selected from the group consisting of alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion**, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, dexamethasone, divalproex, deprenyl, desipramine, dexamethasone, dextroamphetamine, diazepam, disulfram, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, midazolam,

meprobamate, **mirtazapine**, molindone, moclobemide, molindone, **naltrexone**, phenelzine, **nefazodone**, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranylcypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid, **venlafaxine**, and any combination thereof.

DETD . . . anxiety, panic, and phobic disorders, bipolar disorder, borderline personality disorder, behavior control problems, body dysmorphic disorders, cognitive problems, Creutzfeldt-Jakob disease, **depression**, **dissociative** disorders, eating, appetite, and weight problems, edema, fatigue, hiccups, impulse-control problems, irritability, jet lag, mood problems, movement problems, obsessive-compulsive disorder,. . .

DETD . . . anxiety, panic, and phobic disorders, bipolar disorder, borderline personality disorder, behavior control problems, body dysmorphic disorders, cognitive problems, Creutzfeldt-Jakob disease, **depression**, **dissociative** disorders, eating, appetite, and weight problems, edema, fatigue, hiccups, impulse-control problems, irritability, jet lag, mood problems, movement problems, obsessive-compulsive disorder,. . .

DETD . . . on the CNS system of the patient. And, optionally, the drug is selected from the group consisting of alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion**, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, dexamethasone, divalproex, deprenyl, desipramine, dexamethasone, dextroamphetamine, diazepam, disulfram, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, midazolam, meprobamate, **mirtazapine**, molindone, moclobemide, molindone, **naltrexone**, phenelzine, **nefazodone**, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranylcypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid, **venlafaxine**, and any combination thereof.

CLM What is claimed is:

. . . factors affecting medical condition, atypical asthma and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, **bupropion**, pamate, moclobemide, phenalzine, seligeline, **venlafaxine**, carbamazapine, gabapentin, lamotrigine, ginko biloba, dexedrine, methapmphetamine, methylphenidate, and pemoline.

. . . one of anxiety disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, buproprion, **citalopram**, **fluvoxamine**, citalopramine, clomipramine, moclobemide, parnate, phenalzine, seligeline, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, lithium, ginko biloba, kava. . .

. . . childhood, or adolescence and the second treatment is selected from the group consisting of gaba glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, clomiprimine, doxepin, **fluoxetine**, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, trazodone, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clorazepate, diazapam, oxazepam, quazepam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st.. . .

. . . the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, moclobemide,

pamate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, lorazepam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy. . .

. . . amnestic and other cognitive disorders and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, **amitriptyline**, buproprion, fluxotine, moclobemide, parnate, phenalzine, seligeline, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, atenolol, metopolol, propranolol, lithium, ginko biloba, silbtrimin, amantadine, phototherapy at 10000 lux, zolipidem, adderall, dexedrine, methapmphetamine,. . .

. . . not elsewhere classified and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyro sine, donepezil, buproprion, **citalopram**, clomiprimine, desipramine, moclobemide, **nefazodone**, parnate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, ginko biloba, kava kava, silbtrimin, amantadine, phototherapy at 10000. . .

. . . codes and conditions and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, clomiprimine, **fluvoxamine**, moclobemide, notriptyline, parnate, phenalzine, seligeline, trazodone, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hel, clonidine, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy at. . .

. . . the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, moclobemide, pamate, phenalzine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, phototherapy at 10000. . .

. . . sleep disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, buspirone, **citalopram**, clomiprimine, desipramine, **fluoxetine**, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, **sertraline**, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, silbtrimin,. . .

. . . of somatoform disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, buproprion, **citalopram**, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine,. . .

. . . one of substance-related disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, **fluvoxamine**, moclobemide, parnate, phenalzine, seligeline, , **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, atenolol, metopolol, propranolol, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy at. . .

L14 ANSWER 3 OF 12 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN

ACCESSION NUMBER: 2002:5287 ADISCTI
DOCUMENT NUMBER: 800913675
TITLE: Short-term treatment of post-traumatic stress disorder with **naltrexone**: an open-label preliminary study.
ADIS TITLE: **Naltrexone**: therapeutic use.
Post-traumatic stress disorder.
AUTHOR: Lubin G; Weizman A; Shmushkevitz M; Valevski A.
CORPORATE SOURCE: Geha Psychiatric Hospital, Rabin Medical Center, Petah Tikva, Israel.
SOURCE: Human Psychopharmacology: Clinical and Experimental (Jun 1, 2002), Vol. 17, pp. 181-185
DOCUMENT TYPE: Study
REFERENCE: Anxiety Disorders
FILE SEGMENT: Summary

LANGUAGE: English
WORD COUNT: 558

TI Short-term treatment of post-traumatic stress disorder with **naltrexone**: an open-label preliminary study.
ADIS TITLE: **Naltrexone**: therapeutic use.
Post-traumatic stress disorder.

TX Study Message:
Efficacy: **Naltrexone** is not effective in the treatment of patients with post- traumatic stress disorder.
Tolerability: **Naltrexone** is moderately tolerated in patients with post- traumatic stress disorder.

TX Results Highlights:
Efficacy: **Naltrexone** was not effective in the treatment of patients with post-traumatic stress disorder. No clinically significant effects were observed after 2 weeks of **naltrexone** therapy.
Tolerability: **Naltrexone** was moderately tolerated in patients with post- traumatic stress disorder. Three of 8 patients could not tolerate more than 100. . .

TX. . . often resistant to treatment.
It is known that the endogenous opioid system is involved in the pathogenesis of post-traumatic stress disorder. **Naltrexone** is an opioid receptor antagonist that is used in the treatment of drug/alcohol dependence.
This study assessed the efficacy and tolerability of **naltrexone** in the treatment of patients with post-traumatic stress disorder.

TX Author Comments:
`At present it seems that there is no support for the use of **naltrexone** in the treatment of PTSD [post-traumatic stress disorder] patients.'

TX. . . of > 19. Time since trauma was 2-23 (mean 11) years. Five patients also had major depressive disorder.
Concomitant medication: diazepam, **fluoxetine**, oxazepam

TX **Naltrexone**

Drug/Treatment	Dose	Route	Frequency	Duration
Naltrexone	50-200 mg/day	PO	not stated	2 weeks

TX **Naltrexone** was started at 50 mg/day and increased by 50 mg/day every 2 days to a maximum of 200 mg/day depending on tolerability. Three patients could only receive **naltrexone** 100 mg/day while 4 patients received 200 mg/day.

TX Results:

	Naltrexone (n = 7)			
	baseline	week 1	week 2	week 3
Median scores				
Revised PTSD inventory:				
total	88.4	84.6. . .	33.7	33.0
33.0 33.7				
hyperarousal	32.4	30.7 sup(a)	31.0 sup(b)	31.7
Mean scores				
IES scale:				
total	46.0		43.0 sup(a)	45.6
dissociation	59.3		57.1 sup(b)	
58.6				
HDRS score	25.3		23.9	25.1
HARS score	29.3		27.9 sup(b)	29.6

PTSD = Post-traumatic stress disorder; HDRS = Hamilton **Depression** Rating Scale; HARS = Hamilton Anxiety Rating Scale.
a $p < 0.05$ vs baseline; b $0.05 < p < 0.10$ vs. . .

SIDE Side Effects Table:

Side effects (patients)	**Naltrexone** (n = 8)

Weakness/drowsiness	5
Abdominal discomfort/nausea	3
Headache/tremor	1

CT Drug Descriptors: **Naltrexone**, therapeutic use; Drug withdrawal therapies, therapeutic use; Opioid receptor antagonists, therapeutic use
CT Disease Descriptors: Post traumatic stress disorder, treatment;. . .

L14 ANSWER 4 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002364548 EMBASE
TITLE: [Pain perception in self-injurious syndrome]. PERCEPCION DEL DOLOR EN EL SINDROME DE COMPORTAMIENTO AUTOLESIVO.
AUTHOR: Mendoza Y.; Pellicer F.
CORPORATE SOURCE: Dr. F. Pellicer, Subdireccion de Neurociencias, Inst. Nac. Psiq. Ramon de la Fuente, Calzada Mexico-Xochimilco 101, San Lorenzo Huipulco 14370, Mexico. pellicer@imp.edu.mx
SOURCE: Salud Mental, (2002) 25/4 (10-16).
Refs: 62
ISSN: 0185-3325 CODEN: SAMEF5
COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
LANGUAGE: Spanish
SUMMARY LANGUAGE: English; Spanish

AB . . . D1 antagonists and 5HT precursors reduced the incidence of SIB, and NMDA antagonist completely removed it; neither D2 antagonists nor **naloxone** affected SIB. It is possible to generate SIB in rats after inducing peripheral nerve lesions and inflammation process in a. . . significantly correlated with impulsivity, chronic anger and somatic anxiety. A significant negative correlation was found with the number of platelet **imipramine** receptor sites. BPD patients with SIB showed a blunted prolactin response to meta-clorophenylpiperazine that appears to be in inverse relation. . . show lower experimental pain ratings than BPD patients who do experience pain during SIB. They also exhibit higher ratings of **depression**, anxiety, impulsiveness, and **dissociation**, as well as suicide attempts and childhood sexual abuse. The abnormal perception of pain in this group of patients may be related to a tendency to show **dissociative** symptoms. Thus, EEG theta activity in patients that do not feel pain during SIB, is significantly correlated with the **Dissociative** Experience Scale score. Pain perception and **dissociation** Theta rhythm is recorded in hypnotic states as well as during anticipation and control of painful stimulation in healthy individuals.. . . "indifference to pain". On the other hand, left prefrontal mechanisms would inhibit the amygdala resulting in a dampened autonomic output. **Dissociative** symptoms and SIB in BPD patients are common clinical signs. Besides, BPD patients show hypometabolism in prefrontal cortical areas and ACC. It is proposed that the same structures that lead to **dissociative** states may change the perception of pain by cognitive processes. Conclusions The authors hypothesize that the structures involved in processing. . .

CT Medical Descriptors:
*pain
*automutilation
dying
psychosis
mental . . .
compound
caffeine
pemoline
amphetamine
n methyl dextro aspartic acid
opiate
serotonin
dopamine 1 receptor blocking agent
serotonin derivative

n methyl dextro aspartic acid receptor blocking agent
dopamine 2 receptor blocking agent
naloxone
endorphin: EC, endogenous compound
opiate derivative: EC, endogenous compound
opiate antagonist
prolactin: EC, endogenous compound
(3 chlorophenyl)piperazine

RN. . . 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9, 51-62-7, 60-13-9, 60-15-1; (n methyl dextro aspartic acid) 6384-92-5; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (serotonin) 50-67-9; (**naloxone**) 357-08-4, 465-65-6; (endorphin) 60118-07-2; (prolactin) 12585-34-1, 50647-00-2, 9002-62-4; ((3 chlorophenyl)piperazine) 6640-24-0

L14 ANSWER 5 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-25278 DRUGU T
TITLE: Combined treatment with **naltrexone** and EMDR in patients with severe, post-traumatic stress problems.
AUTHOR: Schillen T B; Luethcke H
LOCATION: Dusseldorf, Ger.
SOURCE: Nervenarzt (73, Suppl. 1, S175, 2002)
CODEN: NERVAF ISSN: 0028-2804
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: German
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

TI Combined treatment with **naltrexone** and EMDR in patients with severe, post-traumatic stress problems.

AB. . . case of a young woman with suicidal tendencies and other symptoms arising from traumatic sexual abuse is reported. Treatment with **mirtazapine** + lorazepam + flunitrazepam led to an improvement, but dissociative symptoms persisted. Additional treatment with amisulpride had no effect. Subsequently, long-term treatment with **naltrexone** combined with EMDR trauma therapy led to satisfactory long-term stabilization and the patient improved sufficiently to be released from hospital.. . .

ABEX An 18-yr-old woman with a history of sexual abuse by 5 men at age 12-15 yr presented in a **depressive** state with increasingly suicidal tendencies. Suicide had been attempted by intoxication and wrist cutting at age 14 yr, but there. . . was no evidence of drug abuse. Clinical evaluation revealed sleep disorders, alp-trauma, lack of concentration and hypervigilance. Initial treatment with **mirtazapine**, lorazepam and flunitrazepam led to stabilization with improved sleep. Additional treatment with amisulpride (400 mg/day for 6 wk) had no effect and subsequently the patient developed increasingly severe **dissociative** symptoms with de-realizations, flashbacks and pseudohallucinations. Supplementary treatment with **naltrexone** (50 mg/day for 4 wk) led to complete elimination of **dissociative** symptoms, but anxiety, avoidance behavior, hypervigilance and alp-trauma persisted. The patient improved and was released from hospital after trauma-therapy with EMDR, and remained stable 1 yr later during intensive training and continued treatment with **naltrexone**. (NK/S67)
Kombinationsbehandlung mit Naltrexon und EMDR bei einer Patientin mit schwerer posttraumatischer Belastungsstorung.

CT [01] **NALTREXONE** *TR; SEVERE *TR; POSTTRAUMATIC *TR; STRESS *TR; DEPRESSION *TR; MENTAL-DISORDER *TR; **MIRTAZAPINE** *RC; LORAZEPAM *RC; FLUNITRAZEPAM *RC; AMISULPRIDE *RC; NALTREXON *RN; CASE-HISTORY *FT; IN-VIVO *FT; EMDR *FT; CASES *FT; ANALGESICS *FT; MORPHINE-ANTAGONISTS. . .

L14 ANSWER 6 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2000:137814 USPATFULL
TITLE: Allelic polygene diagnosis of reward deficiency syndrome and treatment
INVENTOR(S): Blum, Kenneth, San Antonio, TX, United States
PATENT ASSIGNEE(S): City of Hope National Medical Center, Duarte, CA, United States (U.S. corporation)
The University of Texas System AMD Board of Regents,

Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6132724		20001017	
APPLICATION INFO.:	US 1998-69886		19980429	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Witz, Jean C.
LEGAL REPRESENTATIVE: Hodgins, Daniel S.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 20845

SUMM . . . Volpicelli et al., 1992). Moreover, ethanol-induced increase of brain dopamine levels in animals is blocked by both opiate receptor antagonists **naloxone** and **naltrexone** (Widdowson and Holman, 1992; Benjamin et al., 1993). A recent review by Gianoukalis and de Waele (1994) support the role. . .

SUMM Pharmacological actions (bromocryptine, **bupropion** and N-propylnorapomorphine) are partly determined by the individual's dopamine D2 genotype. A1 carriers of the DRD2 gene are pharmacologically more. . .

DETD . . . important animal model for RDS behavior. In this regard, various dose regimens and combinations of the three agents (D-phenylalanine [DPA], **naltrexone** [NTX], Ty-D-Arg [TA]) are being employed against self-selection of either alcohol, cocaine, nicotine, cannabis or sugar. The combination of the. . .

DETD . . . salts

DPA + Chromium salts
NTX + Chromium salts
TA + Chromium salts
Chromium salts

DPA = Dphenylalanine; NTX = **naltrexone**; TA = TyD-Arg

DETD . . . Effectiveness Medication Patients

Physicians Effectiveness

Tropamine 190 17 4.00 Trapamine 150 17 3.50
Buspiran 11 2 4.00 Clonidine 15 2 3.00
Nortriptyline 100 3 4.00 Despiramine 8,824 306 2.84
Phenobarbital 2,250 10 4.00 **Imipramine** 2,940 129 2.64
"Benzadiezepines" 155 3 3.33 **Fluoxetine** 2,386 145 2.61
Clonidine 412 15 3.33 L-Tyrosine 350 9 2.60
Chlordiazepoxide 510 14 3.25 Carbamazapine 1,384 86 2.57
Diazepam. . . L-Tryptophan 6,247 110 2.20
Amantadine 19,189 225 2.69 Neuroieptics 1,494 54 2.19
Desipramine 10,352 287 2.65 Naltraxone 1,255 40 2.15
Imipramine 2,885 122 2.48 Phenobarbital 100 3 NR
L-Tryptophan 15,112 198 2.33 Composite of 853 47 2.64
Fluoxetine 1,527 111 2.25 "other drugs"
Bupranarphine 148 19 2.00
Naltrexone 817 31 1.68
Mazindol 11 2 1.00
Composite of "other 8,007 119 3.11
drugs'
TOTALS 79,760 468 2.43 TOTALS 37,156. . .

DETD . . . composition is restricted to the following: Dphenylanine 500 mg per capsule 6.times. day; TyeD-Arg 1 mg per capsule 6.times. day; **Naltrexone** 50 mg per capsule 1 to 3 per day.

*GABRB homozygousity of dinucleotide repeat .gtoreq.185 bp
HTRIA TC polymorphism
HTR2A. . .

DETD TABLE 20

Component for Treatment Composition	Contemplated Effective Dose Range
D-phenylalanine	16 to 5000 mg or
D1-phenylalanine	32 to 10,000 mg
Naltrexone-	1 to 1000 mg
Tyr--Arg	15 .mu.g to 15 mg or Tyr-D-Arg (at same dose range)
Chromium Piccolinate	10 .mu.g. . .

DETD . . . potentials and to drugs. Facilitation of 5HT release can be accomplished with cocaine, (+)-amphetamine, methamphetamine, fenfluramine, parachloramphetamine, clorimipramine (clomipramine) and **amitriptyline**.

DETD Inhibitors of neuronal uptake of 5HT include the tricyclic anti-depressants (**imipramine**, desimipramine, **amitriptyline**, chlorimipramine, **fluvoxamine**; fenfluramine (an anorectic agent) and cocaine. Any 5HT not bound in storage will be converted into metabolites by MAO. However,. . .

DETD Cocaine also affects opiodergic action. With chronic exposure cocaine to rats, dose-dependent alteration of **naloxone** binding was observed. Opiate receptor density was significantly decreased in several brain structures, while it was increased in the lateral. . . appears that opiate binding was specifically affected in "reward centers" and not in other regions (Hammer et al., 1987). Furthermore, **naloxone**, in another study, effectively blocked the threshold lowering action of cocaine in reward centers of the brain (Bain and Korwetsky,. . .

DETD In this example, the effectiveness of interactions of d-Phenylalananine (other enkephalinase inhibitors), Tyr-D-Arg (an enkephalin releaser) and **Naltrexone** (narcotic antagonist) on the release of dopamine into the nucleus accumbens(Acb) of both the Lewis (polydrug preferring) and the Fischer. . . will be given daily doses of three drugs: 500 mg/kg d-phenylalanine (DPA)-1-5 mg/kg of Tyr-D-Arg (TDA) and 1-2 mg/kg of **naltrexone** (NX) (DuPont, Wilmington, Del.) every morning for 18 days. On the 19th day microdialysis sampling will be begun for either. . .

DETD Introduction. Over the last decade, a new rapid method to detoxify either methadone or heroin addicts utilizing the narcotic **naltrexone** (Trexan.RTM., Dupont, Del.) sparked interest in many treatment centers throughout the United States, Canada, as well as many other countries. . .

DETD . . . Gambles as a way of escaping from problems or of relieving a depressed mood (e.g., feelings of helplessness, guilt, anxiety, **depression** 6. Needs to gamble with increasing amounts of money in order to achieve the desired excitement 7. After losing money. . . Acts or feels as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and **dissociative** flashback episodes, including those that occur on awakening and when intoxicated.). 4. Has intense psychological distress at exposure to internal. . .

DETD . . . al., 1991) find that luteal phase platelet 5-HT uptake is decreased in women with PMS or PMDD compared with controls. **Imipramine** binding sites have also been shown to be reduced in women specifically evaluated for PMDD compared with controls during either. . .

DETD . . . conducted to evaluate certain psychoactive drugs for the relief of PMDD and includes antidepressants, including clonipramine (Sunblad et al., 1993) **fluoxetine** (Stone et al., 1991; Wood et al., 1992; Steiner et al., 1995; Brandenberg et al.,; Pearlstein and Stone, 1994), **bupropion** (Pearlstein et al., 1995), **paroxetine** (Eriksson et al., 1995; Yonkers et al., 1996a), maprotiline (Eriksson. et al., 1995), **sertraline** (Yonkers et al., 1996b), nefaxodone

(Girdler et al., 1995), and fenfluramine (Brzezinski et al., 1990).

DETD Bain, et al., "**Naloxone** attenuation of the effect of cocaine on rewarding brain stimulation," Life Sciences, 40:1119-1125, 1986.

DETD Biggio et al., "Stimulation of dopamine synthesis in caudate nucleus by intrastriatial enkephalins and antagonism by **naloxone**," Science, 200:552-54, 1978.

DETD Ehrenpreis, Balagot, Comaty, Myles, "**Naloxone** reversible analgesia in mice produced by D-phenylalanine and hydrocinnamic acid, inhibitors of carboxypeptidase A," In: Bonica et al. (Eds.), Advances.

. .

L14 ANSWER 7 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2003072386 EMBASE
TITLE: Dissociative Identity Disorder: Diagnosis and treatment in the Netherlands.
AUTHOR: Sno H.N.; Schalken H.F.A.
CORPORATE SOURCE: H.N. Sno, Department of Psychiatry, De Heel General Hospital, PO Box 210, 1500 Ee Zaandam, Netherlands
SOURCE: European Psychiatry, (1999) 14/5 (270-277).
Refs: 35
ISSN: 0924-9338 CODEN: EUPSED
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

Ordered thru STIC

AB **Dissociative** Identity Disorder (DID) is a controversial diagnosis and empirical data on the efficacy of treatment modalities are scanty. The objective. . . 1:9. The majority of patients were seen once a week in an outpatient setting. Individual psychotherapy and adjunctive anxiolytic or **antidepressant** medications were the most widely endorsed treatment modalities. Hypnosis was rarely used. We conclude that the diagnosis of DID is. . .

CT Medical Descriptors:
*multiple . . . journal
*anxiolytic agent: DT, drug therapy
*antidepressant agent: DT, drug therapy
*anticonvulsive agent: DT, drug therapy
*neuroleptic agent: DT, drug therapy
*lithium: DT, drug therapy
fluoxetine: DT, drug therapy
paroxetine: DT, drug therapy
serotonin uptake inhibitor: DT, drug therapy
clomipramine: DT, drug therapy
amitriptyline: DT, drug therapy
tricyclic antidepressant agent: DT, drug therapy
oxazepam: DT, drug therapy
alprazolam: DT, drug therapy
clorazepate: DT, drug therapy
diazepam: DT, drug therapy
pimozide: DT, drug therapy
haloperidol: DT, drug therapy
thioridazine: DT, drug therapy
zuclopenthixol: DT, drug therapy
carbamazepine: DT, drug therapy
naltrexone: DT, drug therapy

RN (lithium) 7439-93-2; (**fluoxetine**) 54910-89-3, 56296-78-7, 59333-67-4; (**paroxetine**) 61869-08-7; (clomipramine) 17321-77-6, 303-49-1; (**amitriptyline**) 50-48-6, 549-18-8; (oxazepam) 604-75-1; (alprazolam) 28981-97-7; (clorazepate) 20432-69-3, 23887-31-2; (diazepam) 439-14-5; (pimozide) 2062-78-4; (haloperidol) 52-86-8; (thioridazine) 130-61-0, 50-52-2; (zuclopenthixol) 53772-83-1; (carbamazepine) 298-46-4, 8047-84-5; (**naltrexone**) 16590-41-3, 16676-29-2

L14 ANSWER 8 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1998357499 EMBASE

TITLE: [Dissociative identity disorder in the Netherlands: A survey of diagnosis and treatment by psychiatrists]. DISSOCIATIEVE IDENTITEITSSTOORNIS IN NEDERLAND: DIAGNOSTIEK EN BEHANDELING DOOR PSYCHIATERS.
AUTHOR: Sno H.N.; Schalken H.F.A.
CORPORATE SOURCE: Dr. H.N. Sno, Afdeling Psychiatrie Stichting, Ziekenhuis 'De Heel', Postbus 210, 1500 EE Zaandam, Netherlands
SOURCE: Tijdschrift voor Psychiatrie, (1998) 40/10 (602-614).
Refs: 28
ISSN: 0303-7339 CODEN: TPSYB3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
LANGUAGE: Dutch
SUMMARY LANGUAGE: English; Dutch
AB **Dissociative** Identity Disorder is a controversial diagnosis. Few data are available on the efficacy of treatment modalities. A questionnaire has been. . . majority of the patients is seen once a week in an outpatient setting. Conclusion: Individual psychotherapy and adjunctive anxiolytic or **antidepressant** medications are the most widely endorsed treatment modalities. Hypnosis is rarely used. The diagnosis **Dissociative** Identity Disorder could not be dismissed as a nonsensical notion on the part of a small and local sect of. . .
CT Medical Descriptors:
*multiple . . .
DT, drug therapy
*antidepressant agent: DT, drug therapy
*tricyclic antidepressant agent: DT, drug therapy
*serotonin uptake inhibitor: DT, drug therapy
*anticonvulsive agent: DT, drug therapy
fluoxetine: DT, drug therapy
paroxetine: DT, drug therapy
clomipramine: DT, drug therapy
amitriptyline: DT, drug therapy
haloperidol: DT, drug therapy
pimozide: DT, drug therapy
thioridazine: DT, drug therapy
zuclopenthixol: DT, drug therapy
carbamazepine: DT, drug therapy
lithium: DT, drug therapy
oxazepam: DT, drug therapy
alprazolam: DT, drug therapy
diazepam: DT, drug therapy
naltrexone
RN (**fluoxetine**) 54910-89-3, 56296-78-7, 59333-67-4; (**paroxetine**) 61869-08-7; (clomipramine) 17321-77-6, 303-49-1; (**amitriptyline**) 50-48-6, 549-18-8; (haloperidol) 52-86-8; (pimozide) 2062-78-4; (thioridazine) 130-61-0, 50-52-2; (zuclopenthixol) 53772-83-1; (carbamazepine) 298-46-4, 8047-84-5; (lithium) 7439-93-2; (oxazepam) 604-75-1; (alprazolam) 28981-97-7; (diazepam) 439-14-5; (**naltrexone**) 16590-41-3, 16676-29-2

L14 ANSWER 9 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1993-06573 DRUGU P
TITLE: Characterization of the Binding of (3H)(+)-Pentazocine to Sigma Recognition Sites in Guinea Pig Brain.
AUTHOR: DeHaven Hudkins D L; Fleissner L C; Ford Rice F Y
CORPORATE SOURCE: Sterling-Winthrop
LOCATION: Malvern, Pennsylvania, United States
SOURCE: Eur.J.Pharmacol.Mol.Pharmacol.Sect. (227, No. 4, 371-78, 1992) 3 Fig. 3 Tab. 43 Ref.
CODEN: EJPPET ISSN: 0922-4106
AVAIL. OF DOC.: Sterling Winthrop Pharmaceuticals Research Division, 25 Great Valley Parkway, Malvern, PA 19355-1314, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT; MPC
FILE SEGMENT: Literature

AB. . . of cyclazocine, pentazocine, tonazocine and zenazocine (Sterling-Winthrop), rimcazole (Wellcome), HR-375 (cinuperone, Hoechst-Roussel), BMY-14802 (Bristol-Squibb), dextromethorphan, dextrorphan, PPP-3 (preclamol), 1,3-di(2-tolyl)guanidine, haloperidol, **amitriptyline**, chlorpromazine, **imipramine**, perphenazine, thioridazine, trifluoperazine, triflupromazine, (+)-ethylketo-cyclazocine, GBR-12909, meperidine, morphine, phencyclidine, U-50488H, SCH-23390, SKF-10047, atropine, bethanechol, CPP, apomorphine, d-amphetamine, chlordiazepoxide, clozapine and. . .

ABEX Other drugs studied were (-)-ethylketocyclazocine, glutamate, glycine, methoctramine, MK-801 (dizocilpine), **nalbuphine**, **naloxone**, norbinaltorphimine, pirenzepine, R(-)quinuclidinylbenzilate, SKF-38393, substance-P, sulpiride, U-69593 and yohimbine. The specific binding of 3H-PE to brain membranes of male Hartley. . . maximal at 37 deg, had a KD of 2.9 nM and Bmax of 1998 fmol/mg protein. The half-life for PE **dissociation** was 121 min. PE binding was inhibited by Li+, Ca2+ and Mg2+ (10-100 mM), but not by GTP, GDP, GppNHp,. . . for (-)-butaclamol, which was 10-fold more potent than (+)-butaclamol, and (+)-3PPP, which was 9-fold more potent than (-)-3PPP. Antipsychotics and **antidepressants** showed moderate affinity, with the exception of perphenazine. Dextromethorphan and dextrorphan were moderately potent. Sigma reference compounds interacted with the. . .

[01]. . . TONAZOCINE *RC; ZENAZOCINE *RC; RIMCAZOLE *RC; CINUPERONE *RC; BMY-14802 *RC; DEXTROMETHORPHAN *RC; DEXTRORPHAN *RC; PRECLAMOL *RC; DITOLYLGUANIDINE-1,3 *RC; HALOPERIDOL *RC; **AMITRIPTYLINE** *RC; CHLORPROMAZINE *RC; **IMIPRAMINE** *RC; PERPHENAZINE *RC; THIORIDAZINE *RC; TRIFLUOPERAZINE *RC; TRIFLUPROMAZINE *RC; ETHYLKETAZOCINE *RC; VANOXERINE *RC; PETHIDINE *RC; MORPHINE *RC; PHENCYCLIDINE *RC; U-50488H. . . BETHANECHOL *RC; CPP *RC; APOMORPHINE *RC; AMPHETAMINE *RC; CHLORDIAZEPOXIDE *RC; CLOZAPINE *RC; GLUTAMATE *RC; GLYCINE *RC; METHOCTRAMINE *RC; DIZOCILPINE *RC; **NALBUPHINE** *RC; **NALOXONE** *RC; BUTACLAMOL *RC; NORBINALTORPHIMINE *RC; PIRENZEPINE *RC; RO-2-3308 *RC; SKF-38393 *RC; SUBSTANCE-P *RC; SULPIRIDE *RC; U-69593 *RC; YOHIMBINE *RC; IN-VITRO. . .

L14 ANSWER 10 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1988-43513 DRUGU P
TITLE: Tricyclic Antidepressants Block N-Methyl-D-Aspartate Receptors: Similarities to the Action of Zinc.
AUTHOR: Reynolds I J; Miller R J
LOCATION: Chicago, Illinois, United States
SOURCE: Br.J.Pharmacol. (95, No. 1, 95-102, 1988) 3 Fig. 3 Tab. 33 Ref.
CODEN: BJPCBM ISSN: 0007-1188
AVAIL. OF DOC.: Department of Pharmacological and Physiological Sciences, The University of Chicago, 947 E. 58th Street, Chicago, IL 60615, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB. . . of 3H-MK-801 (Merck-USA) to rat brain membranes was inhibited competitively by cyclazocine, dextrometorphan, ketamine and SKF-10047 and non-competitively by chlorpromazine, **imipramine** (IM), chlorIM (both CIBA-Geigy), **nortriptyline**, amytriptyline, desmethylIM, protriptyline and thioridazine. Carbamazepine, D-amphetamine, mianserin, **fluoxetine**, haloperidol, phenytoin, 5-HT, (+) and (-) oxaprotiline, pargyline, zimelidine, nitrazepam, noradrenaline, maprotiline, dopamine, pentylentetrazol, iprindole, trazodone and **naloxone** were inactive. The MK-801 **dissociation** rate was slowed by chlorIM, IM and desmethylIM. In cultured rat cortical neurons the Ca influx evoked by N-methyl-D-aspartate (NMDA) was reduced by IM, desmethylIM and ketamine.These data show that tricyclic **antidepressants** act on the Zn site of the NMDA receptor.

ABEX. . . IC50 of cyclazocine, ketamine, desmethylIM and IM were 0.091, 0.83, 13.25 and 27.17 uM, resepctively. Binding was also inhibited by **amitriptyline**, chlorpromazine, chlorIM desmethylIM, IM,

nortriptyline, protriptyline and thioridazine with IC50 of 57.25, 45.87, 44.87, 7.41, 22.52, 20.98, 24.9 and 92.45 uM, respectively and Hill slopes somewhat greater than unity. At 100 uM carbamazepine, D-amphetamine, dopamine, **fluoxetine**, haloperidol, iprindol, maprotiline, mianserin, **naloxone**, nitrazepam, noradrenaline, oxaprolidine, pargiline, pentylenetetrazole, phenytoin, 5-HT, trazodone and zimelidine were inactive. The dissociation rate of MK-801 (1/min) was 6250. . .

CT [06] **IMIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; PSYCHOTONICS *FT; IMIPRAMIN *RN; PH *FT
[07] CLOMIPRAMINE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; CLOMIPRAM *RN; PH *FT
[08] **NORTRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; NORTRIPTY *RN; PH *FT
[09] **AMITRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AMITRIPTY *RN; PH *FT
[10] DESIPRAMINE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DESIPRAMI *RN; PH *FT. . . DEXAMPHET *RN; PH *FT
[15] MIANSERIN *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; ANTISEROTONINS *FT; ANTIHISTAMINES-H1 *FT; MIANSERIN *RN; PH *FT
[16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
[17] HALOPERIDOL *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN;. . . IPRINDOLE *RN; PH *FT
[29] TRAZODONE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSEDATIVES *FT; TRAZODONE *RN; PH *FT
[30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
[08] **NORTRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; NORTRIPTY *RN; PH *FT
[09] **AMITRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AMITRIPTY *RN; PH *FT
[10] DESIPRAMINE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DESIPRAMI *RN; PH *FT. . . DEXAMPHET *RN; PH *FT
[15] MIANSERIN *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; ANTISEROTONINS *FT; ANTIHISTAMINES-H1 *FT; MIANSERIN *RN; PH *FT
[16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
[17] HALOPERIDOL *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN;. . . IPRINDOLE *RN; PH *FT
[29] TRAZODONE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSEDATIVES *FT; TRAZODONE *RN; PH *FT
[30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
[16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
[17] HALOPERIDOL *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN;. . . IPRINDOLE *RN; PH *FT
[29] TRAZODONE *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSEDATIVES *FT; TRAZODONE *RN; PH *FT
[30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
[30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT

DDRN . . . OXAPROTIL; CHLORPROM; PARGYLINE; IMIPRAMIN; ZIMELDINE;

CLOMIPRAM; NITRAZPAM; NORTRIPTY; NORADRENA; AMITRIPTY; MAPROTILI; DESIPRAMI; DOPAMINE; PROTRIPTY; PENTETRAZ; THIORIDAZ; IPRINDOLE; CARBAMAZE; TRAZODONE; DEXAMPHET; **NALOXONE**; MIANSERIN; FLUOXETIN

L14 ANSWER 11 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1985-08841 DRUGU T P
TITLE: The Analgesic Effects of Tricyclic/Antidepressants: Clinical and Pharmacological Aspects.
AUTHOR: Devoize J L; Rigal F; Eschalier A; d'Ambrosio A
LOCATION: Clermont-Ferrand, France; Naples, Italy
SOURCE: Presse Med. (13, No. 46, 2806-09, 1984) 31 Ref.
CODEN: PMDAD4
AVAIL. OF DOC.: Service de neurologie, CHU de Clermont-Ferrand, F63000 Clermont-Ferrrand, France.
LANGUAGE: French
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Clinical trials of the use of tricyclic antidepressants (e.g. **imipramine**, **amitriptyline**) in the treatment of chronic pain, and hypotheses concerning the possible mechanism of analgesic action of this group of drugs,. . .

ABEX Results of various clinical studies have confirmed the efficacy of tricyclic **antidepressants** such as **imipramine**, clomipramine, **amitriptyline**, desipramine, doxepin, maprotiline, dibenzepin, in the treatment of chronic pain (lumbalgia, cervicalgia, rheumatic pain, cancer pain, etc.). The best results. . . been obtained using relatively high doses of the drugs and in the treatment of organic pain, particularly peripheral neuropathy. Thus, **imipramine** or **amitriptyline** induced improvement in all cases of diabetic neuropathy whereas diazepam was without effect. **Amitriptyline** has proved effective in the treatment of post-zoster pain. Clomipramine is superior to acetylsalicylic acid in the treatment of peripheral neuropathies. Hypotheses of the possible mechanism of the analgesic action of tricyclic **antidepressants** are discussed. Serotonin, catecholamines and endorphins appear to be involved. Experimental studies with various drugs (**nortriptyline**, protriptyline, **fluoxetine**, zimelidine, indalpine, clomipramine, **amitriptyline**, atropine, methysergide, fenclonine, morphine, **naloxone**, etc.) are reviewed. In contrast with the slow onset of their **antidepressant** effect, these drugs promptly relieve pain, suggesting a **dissociation** of the 2 effects. Combination of tricyclic **antidepressants** with neuroleptics is contraindicated. (Aspects Cliniques et Pharmacologiques de l'Effet Antalgique des **Antidepresseurs** Tricycliques.)

CT [02] **IMIPRAMINE** *TR; **AMITRIPTYLINE** *TR; CLOMIPRAMINE *TR; DESIPRAMINE *TR; DOXEPIN *TR; MAPROTILINE *TR; DIBENZEPIN *TR; DIAZEPAM *TR; ASPIRIN *TR; **NORTRIPTYLINE** *PH; PROTRIPTYLINE *PH; **FLUOXETINE** *PH; ZIMELDINE *PH; INDALPINE *PH; CLOMIPRAMINE *PH; **AMITRIPTYLINE** *PH; ANALGESIC *FT; PH *FT; TR *FT
[03] ATROPINE *PH; METHYSERGIDE *PH; FENCLONINE *PH; MORPHINE *PH; **NALOXONE** *PH; PH *FT
[03] ATROPINE *PH; METHYSERGIDE *PH; FENCLONINE *PH; MORPHINE *PH; **NALOXONE** *PH; PH *FT

L14 ANSWER 12 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 82090639 EMBASE
DOCUMENT NUMBER: 1982090639
TITLE: High-affinity binding of [3H]doxepin to histamine H1-receptors in rat brain: Possible identification of a subclass of histamine H1-receptors.
AUTHOR: Taylor J.E.; Richelson E.
CORPORATE SOURCE: Dept. Psychiat., Mayo Found., Rochester, MN 55905, United States
SOURCE: European Journal of Pharmacology, (1982) 78/3 (279-285).
CODEN: EJPHAZ
COUNTRY: Netherlands

DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
023 Nuclear Medicine
032 Psychiatry
LANGUAGE: English

AB The binding of the radioactively labeled tricyclic **antidepressant**, [3H]doxepin, to rat brain tissue was examined. Scatchard plots of specific [3H]doxepin binding indicated the presence of two distinct binding sites. The equilibrium **dissociation** constant (K(D)) of the high-affinity site was 0.020 nM with a maximal binding capacity (B(max)) of 13.7 fmol/mg protein. The. . . to the high-affinity H1-receptor, however, was approximately 10% of the B(max) obtained using [3H]pyrilamine to label the H1-receptor. Various tricyclic **antidepressants** were very potent inhibitors at the high-affinity [3H]doxepin site. Their potencies, however, did not correlate with their potencies previously reported. . .

CT Medical Descriptors:
*brain
*central nervous system
*doxepin h 3
*mepyramine h 3
rat
in vitro study
animal experiment
***amitriptyline**
*antihistaminic agent
*chlorpheniramine
*desipramine
*diazepam
*diphenhydramine
*doxepin
*histamine h1 receptor
*histamine receptor
***imipramine**
*metiamide
***naloxone**
*protriptyline
drug receptor
radioisotope

RN (**amitriptyline**) 50-48-6, 549-18-8; (chlorpheniramine) 132-22-9; (desipramine) 50-47-5, 58-28-6; (diazepam) 439-14-5; (diphenhydramine) 147-24-0, 58-73-1; (doxepin) 1229-29-4, 1668-19-5; (**imipramine**) 113-52-0, 50-49-7; (metiamide) 34839-70-8; (**naloxone**) 357-08-4, 465-65-6; (protriptyline) 1225-55-4, 438-60-8

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP 2003

L1 1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
L2 1388563 S DEPRESSI? OR ANTIDEPRESS?
L3 670508 S DISSOCIA?
L4 3968 S L2 (S) L3
L5 411408 S OPIATE? OR OPIOID?
L6 2578933 S ANTAGONIS?
L7 233041 S OPIATE? OR OPIOID? (S) ANTAGONIS?
L8 186472 S NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAINE
L9 114 S L4 AND L7
L10 253977 S AMITRIPTYLINE OR LOFEPRAMINE OR BUPROPION OR CITALOPRAM OR FL
L11 8 S L9 AND L10
L12 4049 S L10 AND L8
L13 13 S L4 AND L12

L14 12 DUP REM L13 (1 DUPLICATE REMOVED)

=> dup rem
ENTER L# LIST OR (END):l11
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGLAUNCH, DRUGMONOG2, KOSMET, MEDICONF, NUTRACEUT, PCTGEN, PHARMAML'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L11
L15 7 DUP REM L11 (1 DUPLICATE REMOVED)

=> d l15 1-7 ibib, kwic

L15 ANSWER 1 OF 7 IFIPAT COPYRIGHT 2003 IFI on STN DUPLICATE 1
AN 10343482 IFIPAT;IFIUDB;IFICDB
TITLE: TREATMENT OF REFRACTORY DEPRESSION WITH AN **OPIATE** ANTAGONIST AND AN ANTIDEPRESSANT
INVENTOR(S): Glover; Hillel, New York, NY, US
PATENT ASSIGNEE(S): Unassigned
AGENT: DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP, 2101 L STREET NW, WASHINGTON, DC, 20037-1526, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003087896	A1	20030508
APPLICATION INFORMATION:	US 2001-925190		20010809
FAMILY INFORMATION:	US 2003087896		20030508

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
NUMBER OF CLAIMS: 22
TI TREATMENT OF REFRACTORY DEPRESSION WITH AN **OPIATE** ANTAGONIST AND AN ANTIDEPRESSANT
AB An **antidepressant** or a pharmaceutically acceptable salt thereof, and an **opiate** antagonist or a pharmaceutically acceptable salt thereof, are used to treat refractory **depression** characterized by **dissociation**.
ECLM 1. A method for treating refractory **depression** characterized by **dissociation**, comprising administering to a patient in need thereof an effective **dissociation** reversing amount of an **opiate** antagonist or a pharmaceutically acceptable salt thereof; and an effective **depression** reversing amount of an **antidepressant** or a pharmaceutically acceptable salt thereof.
ACLM 2. The method of claim 1, wherein the **opiate** antagonist is an **opiate** antagonist having a pentacyclic nucleus.
3. The method of claim 2, wherein the **opiate** antagonist is selected from the group consisting of nalmefene, naloxone, naltrexone, nalbuphine, thebaine, and combinations thereof.
4. The method of claim 1, wherein the **opiate** antagonist is selected from the group consisting of kappa **opiate** antagonists, and combinations thereof.
7. The method of claim 1, wherein the **opiate** antagonist or pharmaceutically acceptable salt thereof is administered in combination with a pharmaceutically acceptable carrier.
11. The method of claim 1, wherein the antidepressant is selected form the group consisting essentially of **amitriptyline**, **lofepramine**, **bupropion**, **citalopram**, **fluoxetine**, **fluvoxamine**, **imipramine**, **paroxetine**, **sertraline**, **venlafaxine**, **nefazodone**, **nortriptyline**, **mirtazapine**, **reboxetine**, **SAM-E** and combinations thereof.
12. The method of claim 1, wherein the effective depression reversing amount comprises an initial dosage of **Bupropion** SR in the amount of about 100 mgs. to about 300 mgs. one time daily.
13. The method of claim 1, wherein the effective depression reversing amount comprises a dosage of **Venlafaxine** in the amount of about 75 mgs. per day to about 375 mgs. one time daily.
14. A method for treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need

thereof an effective amount of (a) an **antidepressant**; and (b) an **opiate** antagonist.

15. The method of claim 14, wherein the **opiate** antagonist is an **opiate** antagonist having a pentacyclic nucleus.

16. The method of claim 14, wherein the **opiate** antagonist is selected from the group consisting of nalmefene, naloxone, naltrexone, nalbuphine, thebaine, and combinations thereof.

18. The method of claim 14, wherein the antidepressant is selected form the group consisting essentially of **amitriptyline**, **lofepramine**, **bupropion**, **citalopram**, **fluoxetine**, **fluvoxamine**, **imipramine**, **paroxetine**, **sertraline**, **venlafaxine**, **nefazodone**, **nortriptyline**, **mirtazapine**, **reboxetine**, **SAM-E** and combinations thereof.

19. A method of treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need thereof at least one **opiate** antagonist; evaluating said patient for a response to said **opiate** antagonist; reassessing said patient for **depression**; and administering at least one **antidepressant** to said patient.

20. The method according to claim 19 wherein the step of evaluating said patient for a response to said **opiate** antagonist further comprises the step of evaluating the patient with the Glover Numbing Scale.

. . . 21. The method of according to claim 19 wherein the step of evaluating said patient for a response to said **opiate** antagonist further comprises the step of evaluating said patient for responses selected from the group consisting essentially of numb, hollow,. . .

L15 ANSWER 2 OF 7 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN
ACCESSION NUMBER: 2002:5287 ADISCTI
DOCUMENT NUMBER: 800913675
TITLE: Short-term treatment of post-traumatic stress disorder with naltrexone: an open-label preliminary study.
ADIS TITLE: Naltrexone: therapeutic use.
Post-traumatic stress disorder.
AUTHOR: Lubin G; Weizman A; Shmushkevitz M; Valevski A.
CORPORATE SOURCE: Geha Psychiatric Hospital, Rabin Medical Center, Petah Tikva, Israel.
SOURCE: Human Psychopharmacology: Clinical and Experimental (Jun 1, 2002), Vol. 17, pp. 181-185
DOCUMENT TYPE: Study
REFERENCE: Anxiety Disorders
FILE SEGMENT: Summary
LANGUAGE: English
WORD COUNT: 558

TX. . . with antidepressants, benzodiazepines and, on occasion, antipsychotics. However, many patients are often resistant to treatment. It is known that the endogenous **opioid** system is involved in the pathogenesis of post-traumatic stress disorder. Naltrexone is an **opioid** receptor **antagonist** that is used in the treatment of drug/alcohol dependence.
This study assessed the efficacy and tolerability of naltrexone in the treatment. . .

TX. . . of > 19. Time since trauma was 2-23 (mean 11) years. Five patients also had major depressive disorder.
Concomitant medication: diazepam, **fluoxetine**, oxazepam

TX. . . 33.7 33.0 33.0 33.7
hyperarousal 32.4 30.7 sup(a) 31.0 sup(b) 31.7
Mean scores
IES scale:
total 46.0 43.0 sup(a) 45.6
dissociation 59.3 57.1 sup(b) 58.6
HDRS score 25.3 23.9 25.1
HARS score 29.3 27.9 sup(b) 29.6

PTSD = Post-traumatic stress disorder; HDRS = Hamilton **Depression** Rating Scale; HARS = Hamilton Anxiety Rating Scale.
a p < 0.05 vs baseline; b 0.05 < p < 0.10 vs. . .

CT Drug Descriptors: Naltrexone, therapeutic use; Drug withdrawal therapies, therapeutic use; **Opioid** receptor **antagonists**, therapeutic use

CT Disease Descriptors: Post traumatic stress disorder, treatment; Anxiety, treatment; Anxiety disorders, treatment; Brain disorders, treatment; CNS disorders,. . .

L15 ANSWER 3 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002364548 EMBASE
TITLE: [Pain perception in self-injurious syndrome]. PERCEPCION DEL DOLOR EN EL SINDROME DE COMPORTAMIENTO AUTOLESIVO.
AUTHOR: Mendoza Y.; Pellicer F.
CORPORATE SOURCE: Dr. F. Pellicer, Subdireccion de Neurociencias, Inst. Nac. Psiq. Ramon de la Fuente, Calzada Mexico-Xochimilco 101, San Lorenzo Huipulco 14370, Mexico. pellicer@imp.edu.mx
SOURCE: Salud Mental, (2002) 25/4 (10-16).
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ISSN: 0185-3325 CODEN: SAMEF5
COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
LANGUAGE: Spanish
SUMMARY LANGUAGE: English; Spanish

AB . . . D1-receptor supersensitivity. Adult rats, when administered high doses of caffeine, pemoline or amphetamine, display SIB. The effects of dopamine, NMDA, **opiate**, and serotonin related agents on acute metamphetamine induced SIB in mice, while D1 antagonists and 5HT precursors reduced the incidence. . . since SIB is necessary to maintain a chronic release of endogenous opiods. This hypothesis is supported by the observation that **opiate** antagonists attenuate severe SIB in a subgroup of autistic patients. The dopaminergic system is believed to be responsible for SIB. . . significantly correlated with impulsivity, chronic anger and somatic anxiety. A significant negative correlation was found with the number of platelet **imipramine** receptor sites. BPD patients with SIB showed a blunted prolactin response to meta-clorophenylpiperazine that appears to be in inverse relation. . . show lower experimental pain ratings than BPD patients who do experience pain during SIB. They also exhibit higher ratings of **depression**, anxiety, impulsiveness, and **dissociation**, as well as suicide attempts and childhood sexual abuse. The abnormal perception of pain in this group of patients may be related to a tendency to show **dissociative** symptoms. Thus, EEG theta activity in patients that do not feel pain during SIB, is significantly correlated with the **Dissociative** Experience Scale score. Pain perception and **dissociation** Theta rhythm is recorded in hypnotic states as well as during anticipation and control of painful stimulation in healthy individuals.. . . "indifference to pain". On the other hand, left prefrontal mechanisms would inhibit the amygdala resulting in a dampened autonomic output. **Dissociative** symptoms and SIB in BPD patients are common clinical signs. Besides, BPD patients show hypometabolism in prefrontal cortical areas and ACC. It is proposed that the same structures that lead to **dissociative** states may change the perception of pain by cognitive processes. Conclusions The authors hypothesize that the structures involved in processing. . .

CT Medical Descriptors:
*pain
*automutilation
dying
psychosis
mental . . . isolation
disease severity
animal behavior
dopaminergic system

denervation
peripheral nerve injury
neuritis
ventral tegmentum
electrostimulation
affect
motivation
cingulate gyrus
thalamus anterior nucleus
learning disorder
analgesia
reward
mood
Lesch Nyhan syndrome
human
nonhuman
article
dexamphetamine
noradrenalin: EC, endogenous compound
caffeine
pemoline
amphetamine
n methyl dextro aspartic acid
opiate
serotonin
dopamine 1 receptor blocking agent
serotonin derivative
n methyl dextro aspartic acid receptor blocking agent
dopamine 2 receptor blocking agent
naloxone
endorphin: EC, endogenous compound
opiate derivative: EC, endogenous compound
opiate antagonist
prolactin: EC, endogenous compound
(3 chlorophenyl)piperazine
RN. . . (caffeine) 30388-07-9, 58-08-2; (pemoline) 2152-34-3; (amphetamine) 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9, 51-62-7, 60-13-9, 60-15-1; (n methyl dextro aspartic acid) 6384-92-5; (**opiate**) 53663-61-9, 8002-76-4, 8008-60-4; (serotonin) 50-67-9; (naloxone) 357-08-4, 465-65-6; (endorphin) 60118-07-2; (prolactin) 12585-34-1, 50647-00-2, 9002-62-4; ((3 chlorophenyl)piperazine) 6640-24-0

L15 ANSWER 4 OF 7 USPATFULL on STN
ACCESSION NUMBER: 2000:137814 USPATFULL
TITLE: Allelic polygene diagnosis of reward deficiency syndrome and treatment
INVENTOR(S): Blum, Kenneth, San Antonio, TX, United States
PATENT ASSIGNEE(S): City of Hope National Medical Center, Duarte, CA, United States (U.S. corporation)
The University of Texas System AMD Board of Regents, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6132724		20001017	
APPLICATION INFO.:	US 1998-69886		19980429	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Witz, Jean C.
LEGAL REPRESENTATIVE: Hodgins, Daniel S.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 20845
SUMM . . . establish some of the brain regions and neurotransmitters involved in reward. In particular, it appears that the dependence on alcohol, **opiates** and cocaine relies on a common set of biochemical mechanisms (Cloninger, 1983; Blum, 1978; Blum, 1989). A neuronal circuit deep. . .

SUMM . . . amounts of dopamine from nearby neurons in morphine addicted rats (Nestler et al, 1996). Decreases in D2 receptors observed in **opiate**-dependent subjects have been suggested to indicate that the subjects had low D2 receptors prior to when they began abusing drugs,. . .

SUMM There is evidence that the opoidergic and dopaminergic systems are anatomically and functionally interconnected, suggesting a role for the endogenous **opioidergic** system in mediating the effects of ethanol and other drugs on brain dopaminergic pathways associated with reward. Dopamine **antagonists** and lesions of the dopaminergic pathways in the brain affect pre-proenkephalin A activity (Morris et al., 1988; Normand et al., 1988). Behavioral, pharmacological and neurochemical studies implicate the **opioidergic** and dopaminergic systems in the reinforcing effects of ethanol and other drugs of abuse (Blum et al., 1976a, b; Blum. . . Blum et al., 1977; Blum et al., 1973; Koob and Bloom, 1988; Weiss et al., 1993). Animal studies show that **opiate** receptor agonists increase preference for ethanol, whereas **antagonists** of these receptors reduce ethanol consumption (Blum et al., 1975; Le et al., 1993). Further, studies on animals and human alcoholics suggest the effectiveness of the **opiate** receptor **antagonist** in reducing the positive reinforcing effects of alcohol consumption (O'Malley, 1992; Swift et al., 1994; Blum et al., 1975; Volpicelli et al., 1992). Moreover, ethanol-induced increase of brain dopamine levels in animals is blocked by both **opiate** receptor **antagonists** naloxone and naltrexone (Widdowson and Holman, 1992; Benjamin et al., 1993). A recent review by Gianoukalis and de Waele (1994) support the role of endogenous **opioids** and drugs of abuse (i.e. alcohol).

SUMM Pharmacological actions (bromocryptine, **bupropion** and N-propylnorapomorphine) are partly determined by the individual's dopamine D2 genotype. A1 carriers of the DRD2 gene are pharmacologically more. . . direct microinjection of the D2 agonist N-propylnorapomorphine into the rat nucleus accumbens significantly suppresses the animal's symptoms after withdrawal from **opiates** , while dopamine per se suppresses alcohol withdrawal symptoms (Harris and Aston-Jones, 1994; Blum et al., 1976b). In this regard, there. . . nucleus accumbens and elsewhere in the brain, and it may be that overstimulation of the opioid peptide system by exogenous **opiates** leads to decreases in dopamine function (Pothos et al., 1991). When compared to normal non-alcohol preferring rats, alcohol preferring rats. . .

SUMM . . . appetitive compulsive behaviors are a product of genetic predisposition and environmental insult factors. Numerous studies have implicated the interaction of **opiates**, opioid peptides, CCK-8, glycogen, DA, and insulin in glucose utilization and selective intake of carbohydrates (Morley and Levine, 1988; Moore. . .

SUMM . . . Syndrome (RDS) behaviors in a subject. In certain aspects, this composition includes at least one of the following components: an **opiate** destruction-inhibiting amount of at least one substance which inhibits the enzymatic destruction of a neuropeptidyl **opiate**, the substance being either amino acids, peptides, and structural analogues or derivatives thereof; a neurotransmitter synthesis-promoting amount of at least. . . enkephaline, the enkephaline releaser being, but not limited to, a peptide, and preferably a D-amino acid containing peptide; or an **opiate** antagonist amount of at least one compound which blocks the effects of an **opiate** at either the delta, mu, kappa, sigma, or epsilon receptors. The type of enkephalinase inhibitors, the neurotransmitter precursor, **opiate** destruction-inhibiting substance, **opiate** antagonist, and/or the chromium compound, in addition to the compounds specifically listed above, are further described herein this application and. . .

DETD . . . repeat alleles with a number of different types of drug dependence (cocaine, amphetamine, cannabis), with years of hallucinogen, inhalant, heroin, **opiate**, amphetamine, cocaine, and barbiturate use, with IV drug use and drug overdoses, and with legal problems associated with drug abuse. . .

DETD . . . accumbens, significantly reduces aberrant craving behavior, termed "RDS" behavior, for euphoriant substances to include but not

limited to alcohol, cocaine, **opiates**, nicotine, glucose or other sugars, as well as certain acts such as sexual, gambling, aggression and violence. RDS behaviors have. . .

DETD . . . Effectiveness Medication Patients

Physicians Effectiveness

Tropamine 190 17 4.00 Trapamine 150 17 3.50

Buspiran 11 2 4.00 Clonidine 15 2 3.00

Nortriptyline 100 3 4.00 Despiramine 8,824 306 2.84

Phenobarbital 2,250 10 4.00 **Imipramine** 2,940 129 2.64

"Benzadiezepines" 155 3 3.33 **Fluoxetine** 2,386 145 2.61

Clonidine 412 15 3.33 L-Tyrosine 350 9 2.60

Chlordiazepoxide 510 14 3.25 Carbamazapine 1,384 86 2.57

Diazepam. . . L-Tryptophan 6,247 110 2.20

Amantadine 19,189 225 2.69 Neuroieptics 1,494 54 2.19

Desipramine 10,352 287 2.65 Naltraxone 1,255 40 2.15

Imipramine 2,885 122 2.48 Phenobarbital 100 3 NR

L-Tryptophan 15,112 198 2.33 Composite of 853 47 2.64

Fluoxetine 1,527 111 2.25 "other drugs"

Bupranarphine 148 19 2.00

Naltrexone 817 31 1.68

Mazindol 11 2 1.00

Composite of "other. . .

DETD . . . disorders. Also, see Tables 17-19 for a brief schematic of how certain elements effect reward induced by stimulants (cocaine, etc.), **opiates** and sedative-hypnotics.

DETD . . . homozygos ity of the A1 allele) sedative-hypnotic abuse medical advice rates (AMA), D.sub.2 (Taq A1, B1, exon.sup.6-7 haplotypes, (i.e. alcohol, **opiates**, improved physical and BESS C1) barbiturates) scores DBPC- DATI VNTR (10/10) Outpatient CNRI (homozygosity VNTR for <5 bp repeat MOAA. . . benzodinzipine, Inpatient OT- DAT1 VNTR(9/9) withdrawal (including reduced withdrawal tremors, comparison to D2 TaqI A1, B1, C1 or exon.sup.6-7 alcohol, **opiates**, reduced depression standard detox haplotype barbiturates) meds PHENCAL .TM. Obesity (carbohydrate weight loss, reduced bingeing DBPC - D.sub.2 Taq1 A1,. . . pain or cramps, reduced OT Outpatient Same as for Alcotrol .TM. and headaches, improved overall Cocotrol .TM. mood POMC/Pre-enkephalin/Dynorphin/Orphan **Opiate** receptors delta, sigma, orphan, mu, kappa, epsilon

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.sup.1 Formulas are described in Tables 6 to 17

.sup.2 Alternate composition is. . .

DETD . . . Facilitation

Ventral tegmental area Facilitation

Intracranial Self-Administration

Medial Prefrontal Cortex (Cocaine) Facilitation

Nucleus accumbens (amphetamine) Facilitation

Intravenous Self-Administration

Noradrenaline receptor **antagonists** No change

5-HT receptor **antagonists** Facilitation

M-**opioid** receptor **antagonists** No change
D.sub.1 and D.sub.2 dopamine receptor **antagonists** Inhibition
Noradrenaline denervation (6-hydroxydopamine) No change
5-HT denervation (5,7-dihydroxytryptamine) Facilitation
Dopamine denervation (6-hydroxydopamine)
Nucleus accumbens Inhibition
Ventral tegmental area Inhibition

. . .

DETD TABLE 18

Opiate Reward Paradigm	Effect on Reward
Intracranial Electrical Self-Stimulation	
Lateral hypothalamus	Facilitation
Intracranial Self-Administration	
Nucleus accumbens	Facilitation
Lateral hypothalamus	Facilitation
Ventral tegmental area	Facilitation
Intravenous Self-Administration	
Opioid receptor **antagonists**	
M-receptor **antagonists**	Inhibition
.DELTA.-receptor **antagonists**	No change
K-receptor **antagonists**	No change
Dopainine receptor **antagonists**	Mixed results
Dopamine denervation (6-hydroxydopamine)	
Nucleus accumbens	No change

DETD . . . Reward Paradigm	Effect on Reward
Intracranial Electrical Self-Stimulation	
Lateral hypothalamus	Facilitation
Intracranial Self-Administration	
Ventral tegmental area	Facilitation
Oral Self-Administration	
GABA.sub.A receptor **antagonists**	Inhibition
GABA.sub.A receptor agonists	Facilitation
Opioid receptor **antagonists**	Inhibition
Dopamine receptor **antagonists**	Inhibition
6-HT receptor agonists	Inhibition
Noradrenaline synthesis inhibitors	Inhibition

DETD . . . substance and behavioral disorders. Abused substances and behavioral disorders include, but are not limited to, alcohol, cocaine, nicotine, glucose, Cannabis, **opiates** and **opiate** derivatives, gambling, sexual compulsion, hyperactivity, chronic violent behavior and stress disorders, and also symptoms related to premenstrual syndrome (PMS).

DETD . . . drug
More money spent on All drugs p < 0.01 Comings, et
(including Cocaine and other al., 1994.
Stimulants, except **opiates**)
Age of Onset A1 carriers = 23.2 yrs. vs A2 p < 0.026 Comings, et
carriers = 26.7 yrs. al.,. . .

DETD . . . potentials and to drugs. Facilitation of 5HT release can be accomplished with cocaine, (+)-amphetamine, methamphetamine, fenfluramine, parachloramphetamine, clorimipramine (clomipramine) and **amitriptyline**.

DETD Inhibitors of neuronal uptake of 5HT include the tricyclic anti-depressants (**imipramine**, desimipramine, **amitriptyline**, chlorimipramine, **fluvoxamine**; fenfluramine (an anorectic agent) and cocaine. Any 5HT not bound in storage will be converted into metabolites by MAO. However,. . .

DETD Enhancer/Releaser of Opiod Peptides An aspect of this invention is the use of substances which inhibit the destruction of neuropeptidyl **opiates**. These **opiates** promote the synthesis and release of dopamine. It has been shown that the administration of **opiate**-like substances to animals increases the rate or striatal

DA biosynthesis and metabolism, an effect which is mediated by special **opiate** receptors located on nigrostriatal dopaminergic terminals (Clouet et al., 1970; Biggio et al., 1978; Regiawi, 1980). Upon chronic administration of. . .

DETD Cocaine also affects opiodergic action. With chronic exposure cocaine to rats, dose-dependent alteration of naloxone binding was observed. **Opiate** receptor density was significantly decreased in several brain structures, while it was increased in the lateral hypothalamus. It appears that **opiate** binding was specifically affected in "reward centers" and not in other regions (Hammer et al., 1987). Furthermore, naloxone, in another. . . in reward centers of the brain (Bain and Korwetsky, 1987). Moreover, cocaine appears to affect the analgesic action of certain **opiates** (Misra et al., 1987). The inventors believe that the reinforcing action of cocaine may be mediated in part by **opiate** systems in brain reward centers, which are altered by chronic cocaine exposure.

DETD Narcotic drugs were found to act at various "**opiate** receptors." The brain and other nervous tissue were found to possess endogenous opioids (EO). The related pentapeptides, methionine and leucine-enkephalin. . .

DETD . . . abstinence, similar to those produced by narcotic analgesic drugs when the EO's are administered to man or animals. The endogenous **opiates**, like the narcotic drugs, are members of the class "opioids." Enzymes which degrade enkephalins (E5) are generally called "enkephalinases."

DETD . . . rationale for this is that by doing so the inventors could significantly enhance the effect of enkephalin on its respective **opiate** receptor sites (e.g., delta or mu). To accomplish this aim the inventors would prefer to use the peptide Tyr-Arg (Kyotorphin),. . .

DETD The use of these precursors may be supplemented at appropriate stages of treatment with dopaminergic releasers, blockers, agonists or **antagonists**, or agents affecting the reuptake or degradation of dopamine, norepinephrine or epinephrine. However, and more importantly, the entire range of dopaminergic activity including synthesis, and release is regulated to some degree by certain **opioid** peptides (e.g., enkephalins and endorphins). Centrally administered **opioid** peptides (endorphins and enkephalins) produce elevations in levels of catecholamines in blood plasma in animals and humans (Clouet, 1982). In. . .

DETD . . . use of specific substances, questions were asked about the lifetime use (in years) of alcohol use to intoxication, heroin, other **opiates**/analgesics, barbiturates, other sedatives/hypnotic/tranquilizers, cocaine, amphetamines, cannabis, hallucinogens, and inhalants. For each of the above, where relevant, the subjects were asked. . .

DETD . . . 6.3 58 15.5 38 18.4 6.88 .009
Alcohol dep 160 6.3 98 24.5 22 9.1 non-linear only

---

*OSH = other **opiates** (than heroin or methadone), sedatives and hypnotics

DETD . . . herein. Also, see Tables 17-19 for a brief schematic of how certain elements effect reward induced by stimulants (cocaine, etc.), **opiates** and sedative-hypnotics. Specific examples of the method of treatment combined with genetic diagnosis for RDS behaviors is described below:

DETD EXAMPLE OF ANTI-CRAVING COMPOSITION AND ENHANCEMENT OF COMPLIANCE TO TREXAN.RTM. FOLLOWING RAPID DETOXIFICATION FROM **OPIATES** IN HARDCORE ADDICTS

DETD . . . throughout the United States, Canada, as well as many other countries on a worldwide basis. The dropout rate among hardcore **opiate** addicts even today approaches 90 percent. The basic concept in this rapid method is to provide the patient with a pure narcotic antagonist to block the **opiate**-induced euphoriant effects. Utilizing this approach most patients do not comply and the recidivism rate is over 99% (S. Hall, San. . . contention that the major reason for non-compliance is due to the fact that while the narcotic antagonist (Trexan.RTM.) blocks the **opiate** or

alcohol-induced euphoria (O'Malley et al., 1992; Volpicelli et al., 1992), the drug has little effect on craving behavior. Since. . .

DETD . . . into the study included both male and female patients who were considered hardcore addicts as diagnosed utilizing DSM III for heroin/ **opiate** dependence. Each patient was pre-evaluated by first receiving an injection of 0.4-0.8 mg. Narcan and their withdrawal was assessed (if. . .

DETD Conclusion It is suggested that the addition of the anti-craving formula significantly reduced the craving for **opiates** and, therefore, seems to be important in assisting those hardcore **opiate** addicts in preventing relapse--especially in conjunction with the narcotic antagonist Trexan.RTM..

DETD . . . Gambles as a way of escaping from problems or of relieving a depressed
mood (e.g., feelings of helplessness, guilt, anxiety, **depression**
6. Needs to gamble with increasing amounts of money in order to achieve
the desired excitement
7. After losing money. . . Acts or feels as if the traumatic event were recurring (includes a
sense
of reliving the experience, illusions, hallucinations, and **dissociative**
flashback episodes, including those that occur on awakening and when intoxicated.).
4. Has intense psychological distress at exposure to internal. . .

DETD . . . use of specific substances, questions were asked about the lifetime use (in years) of alcohol use to intoxication, heroin, other **opiates**/analgesics, barbiturates, other sedatives/hypnotics/tranquilizers, cocaine, amphetamines, cannabis, hallucinogens, and inhalants.

DETD . . . 58 15.5 38 18.4 6.88 0.009
Alcohol dep. 160 6.3 98 24.5 22 9.1 non-linear
only

.sup.a OSH = other **opiates** (than heroin or methadone), sedatives and hypnotics.

DETD Invoking a hypothesis that premenstrual symptoms are induced by withdrawal of endogenous **opiates**, several groups have evaluated .beta.endorphin levels in symptomatic women and controls. In a study that included women who retrospectively reported. . .

DETD . . . al., 1991) find that luteal phase platelet 5-HT uptake is decreased in women with PMS or PMDD compared with controls. **Imipramine** binding sites have also been shown to be reduced in women specifically evaluated for PMDD compared with controls during either. . .

DETD . . . conducted to evaluate certain psychoactive drugs for the relief of PMDD and includes antidepressants, including clonipramine (Sunblad et al., 1993) **fluoxetine** (Stone et al., 1991; Wood et al., 1992; Steiner et al., 1995; Brandenberg et al.,; Pearlstein and Stone, 1994), **bupropion** (Pearlstein et al., 1995), **paroxetine** (Eriksson et al., 1995; Yonkers et al., 1996a), maprotiline (Eriksson. et al., 1995), **sertraline** (Yonkers et al., 1996b), nefaxodone (Girdler et al., 1995), and fenfluramine (Brzezinski et al., 1990).

DETD Blum, Hamilton, Wallace, Alcohol and **opiates**: A review of common neurochemical and behavioral mechanisms, Editor: K. Blum, (pp. 203), Academic Press, New York, 1977.

DETD Blum, "A commentary on neurotransmitter restoration as a common mode of treatment for alcohol, cocaine and **opiate** abuse," Integrative Psychiatry, 6:199-204, 1989a.

DETD Li and Chung, "Isolation and Structure of an Untriakontapeptide with **Opiate** Activity from Camel Pituitary Glands," Proc. Nat. Acad. Sci. USA; 73:1145-1148, 1976.

DETD Misra, et al.,; "Stereospecific potentiation of **opiate** analgesia by cocaine: Predominant role of noradrenaline," Pain., 28:129-138, 1987.

CLM What is claimed is:
1. A composition comprising a) an **opiate** destruction-inhibiting amount of at least one substance which inhibits the enzymatic

destruction of a neuropeptidyl **opiate**, said substance being selected from the group consisting of amino acids, peptides, and analogues or derivatives of amino acids or. . .
8. The composition of claim 1 where the **opiate** is a peptide.

9. The composition of claim 1 where the **opiate** is an enkephalin.

L15 ANSWER 5 OF 7 USPATFULL on STN
ACCESSION NUMBER: 2000:80744 USPATFULL
TITLE: Methods and compositions for treating and preventing anxiety and anxiety disorders using optically pure (R) tofisopam
INVENTOR(S): Landry, Donald W., New York, NY, United States
Klein, Donald F., New York, NY, United States
PATENT ASSIGNEE(S): Janus Pharmaceuticals, Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6080736		20000627
APPLICATION INFO.:	US 1999-429503		19991027 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105803P	19981027 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Henley, III, Raymond
LEGAL REPRESENTATIVE: Fish & Neave, Haley, Jr., James F., Shin, Elinor K.
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1332

SUMM In some cases, enantiomers can have opposite pharmacological effects. The (+) enantiomer of picenadol is an agonist at the **opioid** receptor while the (-) enantiomer acts as an **antagonist** at the same receptor. Powell et al. In: Wainer I W, Drager D E, editors, Drug Stereochemistry Analytical Methods and. . . have opposite actions on the receptor. The S-enantiomers are potent activators at L-type voltage-dependant calcium channels whereas the R-enantiomers are **antagonists**. Triggle, D. J. Chirality, 1994: 6:58-62.

SUMM The essential feature of this syndrome is the development of **dissociative** symptoms along with symptoms similar to those of PTSD as a result of exposure to a traumatic event. Individuals with. . . Acute Stress Disorder may neglect basic health and safety needs and are at increased risk of developing PTSD and Major **Depression**.

DETD . . . before, along with, or after other psychoactive compounds, particularly those with antidepressant activity. Such compounds include tricyclic antidepressants such as **amitriptyline**, clomipramine, doxepin, **imipramine**, trimipramine, amoxapine, desipramine, maprotiline, **nortriptyline**, and protryptiline; serotonin-reuptake inhibitors such as racemic **fluoxetine** and enantiomers, **fluvoxamine**, **paroxetine**, **sertraline**, and (.+-.)-**venlafaxine**; atypical antidepressants such as **bupropion**, **nefazodone**, and trazodone; and other monoamine oxidase inhibitors, such as phenelzine, tranylcypromine, and (-)-selgiline, either singly or in combination. In particular,. . .

CLM What is claimed is:
14. The method of claim 13 wherein the tricyclic antidepressant is selected from the group consisting of **amitriptyline**, clomipramine, doxepin, **imipramine**, (+)-trimipramine, amoxapine, desipramine, maprotiline, **nortriptyline**, and protryptiline.

15. The method of claim 12 wherein the antidepressant is selected from the group consisting of **fluoxetine**, **fluvoxamine**,

paroxetine, **sertraline**, (.+-.)-**venlafaxine**, **bupropion**, **nefazodone**, trazodone, phenelzine, tranylcypromine, (-)-selegiline and moclobemide.

L15 ANSWER 6 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 94196592 EMBASE
DOCUMENT NUMBER: 1994196592
TITLE: Pharmacotherapy for post-traumatic stress disorder.
AUTHOR: Sutherland S.M.; Davidson J.R.T.
CORPORATE SOURCE: Department of Psychiatry, Duke University Medical Center, Box 3812,Durham, NC 27710, United States
SOURCE: Psychiatric Clinics of North America, (1994) 17/2 (409-423).
ISSN: 0193-953X CODEN: PCAMDG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . or develop a consensus that is well supported by research findings. What has emerged from the available data is that **antidepressants**, particularly those with serotoninergic properties, are helpful for core PTSD symptoms when given at higher dose levels for at least. . . weeks. The TCAs as a group appear to be effective in amelioration of the intrusive symptoms and of anxiety and **depressive** symptoms, while having little effect on avoidance symptoms. Initial data from studies of the SSRIs suggests that they may have. . . in PTSD symptoms that some patients will no longer meet the diagnostic criteria. The hyperarousal symptoms may respond somewhat to **antidepressants**, but should symptoms continue to be disabling, buspirone or benzodiazepines may be indicated. In choosing a benzodiazepine, those less likely. . . For some patients, phenelzine may be a good choice because it has proven efficacy for the intrusive PTSD symptoms, for **depressive** symptoms, and for some symptoms of autonomic arousal, such as panic attacks. Other agents to be considered for alleviation of. . . impulse control, lithium, beta-blocking drugs, and carbamazepine may be helpful. Brief psychotic episodes should respond to a neuroleptic, although psychoticlike **dissociative** spells may be nonresponsive.

CT Medical Descriptors:
*posttraumatic . . .
therapy
alprazolam: DT, drug therapy
carbamazepine: DT, drug therapy
clonazepam: DT, drug therapy
clonidine: DT, drug therapy
corticotropin releasing factor: EC, endogenous compound
dopamine: EC, endogenous compound
fluoxetine: DT, drug therapy
fluvoxamine: DT, drug therapy
neuroleptic agent: DT, drug therapy
opiate derivative: EC, endogenous compound
phenelzine: DT, drug therapy
propranolol: DT, drug therapy
serotonin: EC, endogenous compound
sertraline: DT, drug therapy
valproic acid: DT, drug therapy

RN (alprazolam) 28981-97-7; (carbamazepine) 298-46-4, 8047-84-5; (clonazepam) 1622-61-3; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (corticotropin releasing factor) 9015-71-8; (dopamine) 51-61-6, 62-31-7; (**fluoxetine**) 54910-89-3, 56296-78-7, 59333-67-4; (**fluvoxamine**) 54739-18-3; (phenelzine) 156-51-4, 51-71-8; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (serotonin) 50-67-9; (**sertraline**) 79617-96-2; (valproic acid) 1069-66-5, 99-66-1

L15 ANSWER 7 OF 7 ADISNEWS COPYRIGHT (C) 2003 Adis Data Information BV on STN

ACCESSION NUMBER: 1997:10 ED: 8 Aug 2001 UP: 8 Aug 2001
DOCUMENT NUMBER: 11738324-800458311
TITLE: Reviews: Headline news of 1996 - Part 3.
SOURCE: INPHARMA 10 Jan 1997 ISSN: 1173-8324
DOCUMENT TYPE: (MIX)
WORD COUNT: 1137

TX. . . local anaesthetic to be used when profound muscle relaxation is required during surgery. Also, low-dose ropivacaine is associated with greater **dissociation** of the sensory and motor effects of local anaesthesia, compared with other local agents such as bupivacaine; this allows for. . . the agent are currently underway.

Remifentanil [`Ultiva'; Glaxo Wellcome], the first of a new class of anaesthetic drugs called the esterase-metabolised **opioids**, was approved in its first market, Germany, last year. Remifentanil is indicated for use during the induction and maintenance of. . . the end of 1996, and was subsequently launched in UK in October.

The use of alternative medicines in the treatment of **depression** was another focus of 1996. In particular, interest has centred on extracts of St John's Wort (Hypericum perforatum). A meta-analysis of randomised trials involving patients with anxiety, **depressive** and sleep disorders indicated a response rate of 55% to Hypericum perforatum therapy, compared with a response rate of 22% with placebo The response rate achieved with Hypericum perforatum therapy was comparable to that achieved with conventional **antidepressants**.

Another study, involving 165 patients with **depression** demonstrated that hypericum extract [LI-160; Lichtwer Pharmaceuticals] had comparable **antidepressant** activity to **amitriptyline** after 6 weeks' therapy. Furthermore, hypericum extract was shown to have a better tolerability profile than **imipramine** in another 209-patient study.

GENITOURINARY MEDICINE

Merck & Co. contested the results of a study, published in 1996, which showed that their. . . postmenopausal women with RA. Nine women received intra- articular injections of genetically altered synovial cells that express an IL-1 receptor **antagonist**.

T-cell receptor Vbeta17 peptide vaccine [Immune Response; phase I/II] was also under investigation in patients with RA. The 15 vaccine recipients. . .

RN 50-48-6 (**AMITRIPTYLINE**)
50-49-7 (**IMIPRAMINE**)
52-86-8 (HALOPERIDOL)
8001-02-3 (CORTICOSTEROIDS)
38396-39-3 (BUPIVACAINE)
63590-64-7 (TERAZOSIN)
66376-36-1 (ALENDRONIC ACID)
71125-38-7 (MELOXICAM)
84057-95-4 (ROPIVACAINE)
89957-37-9 (ANTIBODIES)
98319-26-7 (FINASTERIDE)
106516-24-9. . .

=> s psychosis
L16 152084 PSYCHOSIS

=> s refractory depression
L17 1677 REFRACTORY DEPRESSION

=> s l16 and l17
29 FILES SEARCHED...
L18 129 L16 AND L17

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,

EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP 2003

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L1       1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
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L5        411408 S OPIATE? OR OPIOID?
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L8        186472 S NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAINE
L9           114 S L4 AND L7
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L11            8 S L9 AND L10
L12         4049 S L10 AND L8
L13           13 S L4 AND L12
L14           12 DUP REM L13 (1 DUPLICATE REMOVED)
L15            7 DUP REM L11 (1 DUPLICATE REMOVED)
L16       152084 S PSYCHOSIS
L17         1677 S REFRACTORY DEPRESSION
L18          129 S L16 AND L17

=> s l16 (s) l17
L19            5 L16 (S) L17

=> s l7 and l19
L20            0 L7 AND L19

=> s l18 and l7
L21            1 L18 AND L7

=> d l21 ibib, kwic

L21   ANSWER 1 OF 1  DRUGU  COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-01884  DRUGU   T
TITLE:            Treatment augmentation with opiates in severe and
                  refractory major depression.
AUTHOR:           Stoll A L; Rueter S
LOCATION:         Belmont, Mass., USA
SOURCE:           Am.J.Psychiatry (156, No. 12, 2017, 1999) 2 Ref.
                  CODEN: AJPSAO       ISSN:  0002-953X
AVAIL. OF DOC.:   No Reprint Address.
LANGUAGE:         English
DOCUMENT TYPE:    Journal
FIELD AVAIL.:     AB; LA; CT
FILE SEGMENT:     Literature
TI    Treatment augmentation with opiates in severe and refractory
      major depression.
AB    3 Cases of refractory depression treated with the mu
      opiate agonists oxycodone and oxymorphone were reported in a
      letter.  Patients with refractory depression reported
      lifting of symptoms during opiate abuse or treatment.  Their
      depression responded well to supervised oxycodone or oxymorphone
      treatment.  Opiates should be considered in carefully selected
      patients with severe, refractory depression.
ABEX.  . .  A 44-yr-old man with severe, chronic depression had not responded
      well to antidepressant treatment. He also had a history of opiate
      abuse and reported a lack of depression whilst using opiates.
      He was given a trial of oxycodone 10 mg/day under supervision, and
      remained in remission from depression after 18 mth, without emergence of
      opiate abuse or tolerance. A 45-yr-old woman with a history of
      bipolar disorder and opiate abuse (in remission for 2 yr)
      showed a lack of response to mood stabilizers, and emergence of mania
      under standard antidepressant treatment.  She reported feeling well when
      taking opiates, particularly oxymorphone.  Oxymorphone 8 mg/day
      was added to lamotrigine therapy, and she remained well for 20 mth
      without emergence of opiate abuse or tolerance. A 43-yr-old man
      with a history of chronic major depression refractory to antidepressants,
      reported that he had shown marked improvement whilst receiving
```

opiates after a dental procedure.He was started on oxycodone 10
mg t.i.d. for 9 mth, and showed a marked antidepressant response without
opiate abuse or tolerance. (KO)
CT DEPRESSION *TR; REFRACTORY *TR; BIPOLAR *TR; **PSYCHOSIS** *TR;
MENTAL-DISORDER *TR; CASE-HISTORY *FT; IN-VIVO *FT; NARCOTIC *FT;
ANTIDEPRESSANT *FT; ADDICTION *FT; CASES *FT; PSYCHOSTIMULANT *FT
CT DEPRESSION *TR; REFRACTORY *TR; BIPOLAR *TR; **PSYCHOSIS** *TR;
MENTAL-DISORDER *TR; CASE-HISTORY *FT; IN-VIVO *FT; NARCOTIC *FT;
ANTIDEPRESSANT *FT; ADDICTION *FT; CASES *FT; PSYCHOSTIMULANT *FT

=> dup rem
ENTER L# LIST OR (END):l19
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGLAUNCH,
DRUGMONOG2, KOSMET, MEDICONF, NUTRACEUT, PCTGEN, PHARMAML'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L19
L22 5 DUP REM L19 (0 DUPLICATES REMOVED)

=> d l22 1-5 ibib, kwic

L22 ANSWER 1 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2002:228330 USPATFULL
TITLE: Combination treatment for anxiety, depression,
obsessive compulsive disorder and psychosis
INVENTOR(S): Howard, Harry R., JR., Bristol, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002123490	A1	20020905	
APPLICATION INFO.:	US 2001-10651	A1	20011206	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-272619P	20010301 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49,
NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
LINE COUNT: 1659
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0006] This invention also relates to a method of treating OCD,
psychosis and depression in a mammal, comprising administering
to said mammal: (a) a serotonin reuptake inhibitor (SRI) compound that
exhibits activity. . . and "b" above are present in amounts that
render the combination of the two agents effective in treating,
respectively, OCD, **psychosis** and depression with improvement
in the efficacy achieved by either component individually in the
treatment of OCD, depression, especially **refractory**
depression, and **psychosis**.
SUMM . . . invention that contain an atypical antipsychotic agent and an
SRI antidepressant are useful for the treatment of OCD, depression,
especially **refractory depression**, or
psychosis, especially schizophrenia. As used herein, the term
"depression" includes depressive disorders, for example, single episodic
or recurrent major depressive disorders,. . .
SUMM [0010] The compositions of the present invention are especially useful
for the treatment of depression, especially **refractory**
depression where the use of an antidepressant is generally
prescribed. By the use of a combination of an atypical antipsychotic
agent and an SRI antidepressant agent in accordance with the present
invention, it is possible to treat depression, especially
refractory depression, in patients for whom
conventional antidepressant therapy might not be wholly successful or
where OCD or **psychosis**, especially schizophrenia, are present.

L22 ANSWER 2 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-46795 DRUGU T
TITLE: The influence of clinical features of refractory depression on antidepressant treatment results.
AUTHOR: Hese R T; Gruszczynski W; Szwed A; Kielc M; Zalitacz M
CORPORATE SOURCE: Univ.Silesian
LOCATION: Katowice, Lodz; Bytom, Pol.
SOURCE: Pharmacopsychiatry (35, No. 5, III, 2002) 1 Ref.
CODEN: PHRMEZ ISSN: 0176-3679
AVAIL. OF DOC.: Silesian University School of Medicine, Department of Psychiatry, Katowice, Poland.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The therapeutic efficacy of amitriptyline (AMI), mianserin (MIA) and ECT were compared in 180 patients with **refractory depression** treated at a Polish hospital. Patients with moderate depression, **psychosis**-free depression and depression with inhibition features had better therapeutic results than those with severe depression, psychotic depression and depression with. . .

L22 ANSWER 3 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-22698 DRUGU T
TITLE: Treatment-refractory depression successfully treated with the combination of mirtazapine and lithium.
AUTHOR: Moustgaard G
LOCATION: Helsingborg, Swed.
SOURCE: J.Clin.Psychopharmacol. (20, No. 2, 268, 2000) 7 Ref.
CODEN: JCPYDR ISSN: 0271-0749
AVAIL. OF DOC.: S-25187 Helsingborg, Sweden.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A case of **refractory depression** successfully treated with the combination of mirtazapine (MZ) and lithium (Li) in a patient, who was previously treated with several. . . and was treated with the combination of amitriptyline and neuroleptics. After several yr, the patient was again admitted due to **psychosis** and suicidal thoughts. Zuclopenthixol (ZC) alone, ECT combined with thioridazine (TR) and ZC, and fluoxetine (FX) combined with Li produced. . .

L22 ANSWER 4 OF 5 JICST-EPlus COPYRIGHT 2003 JST on STN
ACCESSION NUMBER: 960607740 JICST-EPlus
TITLE: Endocrinological treatment for **refractory depression**, manic-depressive illness, schizoaffective disorder and residual state of acute **psychosis**.
AUTHOR: KITAYAMA ISAO; HAMANAKA KENJI; INUI KOJI; MOTOMURA HIDEFUMI; NOMURA JUN'ICHI
KAWAKITA MASAHIKO
CORPORATE SOURCE: Mie Univ., Sch. of Med.
Miekenkoseinogyokyodokumiairengokai Suzukachuosogobyoin
SOURCE: Kanjo Shogai no Shinkei Kagakuteki Seiin oyobi Chiryo ni kansuru Kenkyu. Heisei 7 Nendo Kenkyu Hokokusho (Neuroscientific Research on Pathogenesis and Treatment of Affective Disorders), (1996) pp. 93-95. Journal Code: N19961642 (Tbl. 2, Ref. 2)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
TI Endocrinological treatment for **refractory depression**, manic-depressive illness, schizoaffective disorder and residual state of acute **psychosis**.

L22 ANSWER 5 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1987-18119 DRUGU T S

TITLE: The Use of Psychostimulants in General Psychiatry. A Reconsideration.
AUTHOR: Chiarello R J; Cole J O
LOCATION: Belmont, Massachusetts, United States
SOURCE: Arch.Gen.Psychiatry (44, No. 3, 286-95, 1987) 1 Fig. 2 Tab. 81 Ref.
CODEN: ARGPAQ ISSN: 0003-990X
AVAIL. OF DOC.: McLean Hospital, Belmont, MA 02178, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
ABEX. . . DA, and DA and MP have been successfully used as adjuvants to tricyclic antidepressants or MAO inhibitors in patients with **refractory depression** without inducing hypertensive crises or other serious side effects. Side effects of psychostimulants include anorexia, stereotypy, an increase in spontaneous and conditioned motor behavior and acute paranoid **psychosis**. (E28/PMI)

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP 2003

L1 1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
L2 1388563 S DEPRESSI? OR ANTIDEPRESS?
L3 670508 S DISSOCIA?
L4 3968 S L2 (S) L3
L5 411408 S OPIATE? OR OPIOID?
L6 2578933 S ANTAGONIS?
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L8 186472 S NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAINE
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L11 8 S L9 AND L10
L12 4049 S L10 AND L8
L13 13 S L4 AND L12
L14 12 DUP REM L13 (1 DUPLICATE REMOVED)
L15 7 DUP REM L11 (1 DUPLICATE REMOVED)
L16 152084 S PSYCHOSIS
L17 1677 S REFRACTORY DEPRESSION
L18 129 S L16 AND L17
L19 5 S L16 (S) L17
L20 0 S L7 AND L19
L21 1 S L18 AND L7
L22 5 DUP REM L19 (0 DUPLICATES REMOVED)

=> s l19 and l8
L23 0 L19 AND L8

=> s refractory depression with dissociation
75% OF LIMIT FOR L#S REACHED
28 FILES SEARCHED...
L24 0 REFRACTORY DEPRESSION WITH DISSOCIATION

=> s refractory depression with dissocia?
28 FILES SEARCHED...
L25 0 REFRACTORY DEPRESSION WITH DISSOCIA?

=> s refractory depression
L26 1677 REFRACTORY DEPRESSION

=> s depersonalization or dissociat? or detachment or alexithymia or no feeling?
18 FILES SEARCHED...

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L27     883287 DEPERSONALIZATION OR DISSOCIAT? OR DETACHMENT OR ALEXITHYMIA OR
               NO FEELING?

=> s l26 and l27
L28          17 L26 AND L27

=> s l8 and l10
 95% OF LIMIT FOR L#S REACHED
L29        4049 L8 AND L10

=> s l28 and l29
MAXIMUM L# WOULD BE EXCEEDED.

=> s l28 and l29
MAXIMUM L# WOULD BE EXCEEDED.

=> d his

     (FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
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L17        1677 S REFRACTORY DEPRESSION
L18         129 S L16 AND L17
L19           5 S L16 (S) L17
L20           0 S L7 AND L19
L21           1 S L18 AND L7
L22           5 DUP REM L19 (0 DUPLICATES REMOVED)
L23           0 S L19 AND L8
L24           0 S REFRACTORY DEPRESSION WITH DISSOCIATION
L25           0 S REFRACTORY DEPRESSION WITH DISSOCIA?
L26        1677 S REFRACTORY DEPRESSION
L27      883287 S DEPERSONALIZATION OR DISSOCIAT? OR DETACHMENT OR ALEXITHYMIA
L28          17 S L26 AND L27
L29        4049 S L8 AND L10
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